DECLARATION OF RUBEN C. GUR, PH.D.

I, Ruben C. Gur, Ph.D., state the following: EA

1. I am a neuropsychologist, with a special focus on imaging applications to the diagnosis and study of people with behavioral disturbances associated with brain dysfunction. I have been requested by counsel for Toronto Patterson to submit this affidavit in support of a state habeas corpus petition to be filed on behalf of Mr. Patterson on or about Monday, July 29, 2002. Mr. Patterson currently is scheduled to be executed by the State of Texas on August 28, 2002. My opinion is that the human brain is not fully mature before reaching adulthood, and that furthermore the brain regions that are the most important for regulating impulse control, planning, consideration of consequences, abstract reasoning and, most probably, moral judgment, are the very regions that mature last. This declaration details my background, identifies the bases for my opinion, and presents my expert opinion.

Synopsis of Curriculum Vitae

2. My Curriculum Vitae is attached to this declaration. My qualifications for the opinions I state in this declaration include the following:

a. I have been licensed as a psychologist in Pennsylvania since 1976. I received a B.A. from the Hebrew University of Jerusalem and an M.A. and a Ph.D. in Clinical Psychology from Michigan State University. I completed Postdoctoral Fellowships at Stanford University and at the University of Pennsylvania.

b. I am a Diplomate of the American Board of Professional Psychology, with Specialty in Clinical Neuropsychology (ABPP/CN).

c. I am, or have been, a member of the American Psychological Association, Division of Physiological and Comparative Psychology (Fellow status), Division of Neuropsychology

(Fellow), the American Psychological Society (Fellow), the American College of Neuropsychopharmacology (Fellow), the American Association for the Advancement of Science, the International Neuropsychological Society, the National Academy of Neuropsychologists, the New York Academy of Science, and the John Morgan Society.

d. Among other honors, I have received the Erikson Award for Scientific Excellence and the 1990 Stephen V. Logan Award from the National Alliance for the Mentally Ill. I have authored or co-authored refereed publications in peer-reviewed journals, made national and international presentations in the field of imaging and brain dysfunction, have served and am serving on Editorial Boards of professional journals, have served on Search Committees for journal Editorship, and have reviewed manuscripts for leading journals in the areas of imaging, brain and behavior, and schizophrenia, have served on Advisory Panels and Study Sections of the National Institutes of Health and currently serve on the NIH Review Group on "Clinical Neuroscience and Biological Psychopathology." I have contributed chapters to textbooks and other scholarly volumes on the topic of brain imaging and neuropsychology.

e. I have the academic rank of Professor (with Tenure) on the Standing Faculty of the University of Pennsylvania, with a primary appointment in Psychiatry and secondary appointments in Neurology and in Radiology. I am currently the Chief of the Brain Behavior Laboratory (BBL) and Director of Neuropsychology, Department of Psychiatry at the Hospital of the University of Pennsylvania. I am Principal Investigator of the Neuropsychology Core and the Functional Imaging Core of the Federally funded Schizophrenia Center, Co-PI of the functional MRI project of the Conte Center for Neurosciences, and PI, Co-PI and investigator on several individual NIH grants (RO1s) on brain imaging and psychopathology. I also supervise interns and practicum students in neuropsychology. I am advisor of the Biological Basis of Behavior

Undergraduate Major Program at the University of Pennsylvania. Additionally, I am a supervisor of postdoctoral Fellows and doctoral students in Psychology and Neuroscience and Co-PI of a Federally funded Training Program in the behavioral neurosciences.

f. I have been recognized as an expert and allowed to testify with respect to my expert opinions in the specialty of Neuroimaging and Neuropsychology in state and Federal courts.

The basis for the opinion stated in 1

3. The brain is a complex organ, as could be expected from the complexity of human behavior, and lacking tools for studying the living brain has made scientific progress slow and laborious. However, methods developed in the '70s and implemented in the '80s have yielded powerful tools for obtaining reliable measures of brain structure, function and behavior. By the mid-'90s these methods have become standard in the assessment of brain structure and function.

a. During the Month of June, 2002, I have reviewed the published literature on the topic of brain maturation in humans. I have reached the opinion stated in point 1 based on that review.

b. The purpose of the review was to summarize current understanding of the process of maturation in human brains during the juvenile period and up to young adulthood. Below I will describe the methods used in such investigations and outline the main findings regarding the course of brain development. Of course there is much that we do not know about brain maturation, but there is congruence of evidence indicating that brain maturation is not complete until young adulthood (about age 21). Furthermore, the main index of maturation, which is rate of myelination, points to large variability in

the rate of maturation among brain regions. In general, maturation of association cortex is not complete even by late adolescence and within this cortex the prefrontal regions are last to mature. The review will conclude by discussing the behavioral implications of these findings. The role of myelination is to focus and refine the operation of neural networks regulating behavior, and the frontal lobes specifically modulate and inhibit impulses, shaping behavior in accordance with planned action and long-term goals. Therefore, the brain anatomy data indicate that people are not biologically prepared to exercise mature frontal lobe control until they reach adulthood.

c. The rate at which the human brain matures has been of considerable interest to neuroscientists and knowledge on when different brain regions mature during human development may have profound implications for understanding behavioral development. Although the brain and its structure become well differentiated during fetal development, there is overwhelming evidence that much of the brain maturational process occurs after birth. Indeed, projections from early pioneering work on donated brain tissue have indicated that some brain regions do not reach maturity in humans until adulthood. These projections have been confirmed by more recent studies using neuroimaging with advanced methods for soft tissue segmentation and regional parcellation. Here I will first describe the initial neuroanatomic methods and results they produced, which gave rise to hypotheses currently being confirmed and further refined. I will proceed to explain the novel methods using structural and functional neuroimaging, and summarize results pertinent to the issue of brain maturation. I will

conclude by an attempt to integrate findings from the diverse methods and explain their implications to behavior, focusing on issues pertinent to criminal responsibility

d. Initial studies: Post-mortem tissue anatomy. While sophisticated methods for preservation and dissection of post mortem brain tissue had been developed in the first decades of the twentieth century, it was not until the 1960's that enough such tissue was available to examine the question of brain maturation in humans. Arguably the largest collection and the most influential work was that of Professor Paul I. Yakovlev and his colleagues at Harvard University. His methods, findings and conclusions have been summarized in a landmark chapter titled "The myelination cycles of regional maturation of the brain" co-authored with Dr. André-Roch Lecours, which was published in a book on Regional Brain Development in Early Life (edited by Prof. Alexandre Minkowski and published by Blackwell Scientific Publications, Oxford, England, 1967).

e. The anatomic work has focused on the process of the creation of fatty tissue surrounding nerve fibers, which is known as "myelogenesis." Myelogenesis is important for assuring efficient transmission of neuronal signals. The fatty tissue called myelin surrounds the nerve fibers that carry information across large distances very much in the same way that rubber is used for insulating cables designed to conduct electricity across distance. The process can be examined by obtaining slices of brain tissue from a wide age range, treated in a way that enables visualization of myelin, and comparing its abundance. Such treatment of tissue is called "staining," and Yakovlev and his colleagues used a staining method developed in the twenties by Loyez. The method relies on the ability to observe both the density of stained fibers and the

intensity of coloration (light to dark gray and blue to black), and these can be used to index degree of myelination (see Figure 1).

f. Yakovlev and his colleagues examined over 200 brains ranging in age from fourth fetal month to one postnatal year, and another large set of brains from the third decade of life on. Unfortunately they had very few brains from the first and second decades of life, and their extrapolations for that phase of development are accordingly more tentative. Nonetheless, They were able to derive some principles and propose hypotheses that were confirmed with remarkable consistency using current techniques.

The main surprise was the much slower progression of the maturational process in the human brain compared to what had been expected from animal studies. Yakovlev and his colleagues have carefully charted the maturational process for a large set of regions and found some that matured very early while others were far from maturation at one year of age. By extrapolating from the sample of adult brains and the few specimens from the period in between, they have produced "maturation charts" for these brain regions (Figure 2). Based on these charts they identified several principles. One of the main principles is illustrated in Figure 3. The brain can be conceptualized architecturally (and phylogenetically) as consisting of three "zones": the median (median thalamus and hypothalamus, septum, hippocampus) the paramedian (limbic) and the supralimbic (mostly cerebral cortex). They noted that maturational rate is fastest for the paramedian zone, where it is complete within the first decade of life, and slowest for the cortical regions where development seems to extend into adulthood.

This principle has rather profound implications for behavior, and is consistent with behavioral data on development. The region that is slowest to mature is the part of the

brain that basically serves to inhibit and modulates more primitive, drive related activation of the limbic areas. From a phylogenetic perspective, the brain areas that are latest to mature are those areas that have seen the greatest expansion in humans and are associated with faculties such as language comprehension and expression, abstraction and reasoning, comprehension and expression of emotions, impulse control and planning, and aspects of attention and memory (including working memory). Thus, the anatomic data as interpreted by Yakovlev and his colleagues indicated that the very functions that make us uniquely human are the latest to become fully integrated into the workings of the developing brain.

g. Other contributions of anatomic studies for understanding brain development ranged from gross measurement of brain weight in large samples to more detailed measurements of synaptic processes in small samples. For example, Dekaban and Sadowsky (1978) tabulated body and brain weight in nearly 5000 autopsy reports, ranging in age from weeks to 90 years, and plotted these values against age. The most important result from the perspective of this review is that brain weight did not reach its peak until about age 20, and showed steady decline thereafter (see Figure 4). This method, of course, could not distinguish myelin from other tissue and hence does not directly examine maturation.

h. Using methods for examining synaptic density, Prof. Peter Huttenlocher from the University of Chicago was able to uncover another neurodevelopmental phenomenon apparently taking place during adolescence: "pruning." Specifically, he observed a decline in the density of synapses between ages 2 and 16 accompanied by a decrease in neuronal density. His conclusion required a considerable leap of imagination, since he only had one specimen between the ages of 8 and 20 years, however it made

theoretical sense and was consistent with animal studies. According to the pruning hypothesis, at some point during adolescence neurons and their connections that have not been consistently used during childhood "shrivel off" and are eliminated, thereby allowing for greater efficiency of the remaining neural systems (Huttenlocher, 1979; Huttenlocher et al., 1982).

i. Current anatomic studies: Structural imaging with MRI. The post-mortem tissue studies such as conducted by Yakovlev and his colleagues have contributed important insights into understanding brain maturation, but they have serious limitations. Most importantly, tissue availability depends on sources that may bias the age ranges available; the inability to quantify the measures in an automated fashion limits the number of brains and regions that can be examined; there is large variation introduced by fixation and staining methods; and it is impossible to do repeated studies in the same individual to trace developmental changes.

j. All these difficulties are circumvented by a set of novel techniques developed in the 1970s and fully implemented by the 1990s, and that can be generally referred to as "structural imaging". These methods permit visualization and volumetric measurement of brain structure in living people without risk. The method that has become state of the art for these studies is based on magnetic resonance imaging (MRI) procedures. The head is placed in a strong magnetic field (current standard is at 1.5 tesla), and the image is based on recording the resonance of molecules after perturbations with radiofrequency (RF) signals using special coils. Recordings are made with antennae, very much like recording of radio waves. What makes MRI particularly amenable for quantitative analysis is that different echo times can

highlight different soft tissue contrasts, procedures that have similar effects to those of staining in post mortem studies. The main potential drawback in MRI is the difficulty of maintaining a homogeneous field strength throughout the image brain. Inhomogeneity will produce "shading" effects, which can be sometimes compensated for by the clinician but have to be minimized, or compensated for by complex statistical operation, when trying to implement a computer algorithm to identify the tissue. Several approaches have been developed in the early 90s, and these have now become standard and have been shown to produce reliable results both in phantom and in human studies (e g., Filipek, Richelme, Kennedy, and Caviness, 1994; Kohn et al, 1991; Yan and Karp 1994). These methods have provided data on the intracranial composition of the three main brain compartments related to cytoarchitecture and connectivity: gray matter (GM) - the somatodendritic tissue of neurons (cortical and deep), white matter (WM) - the axonal compartment of myelinated connecting fibers, and cerebrospinal fluid (CSF). An example of computerized segmentation of MRI into these compartments is provided in Figure 5.

k. It has taken some time to apply these segmentation methods to a sufficiently large sample of healthy people across the age range so as to examine maturational processes. However, several groups have made considerable progress and the results of their efforts, while still tentative with regard to precise charting of developmental trajectories for all brain regions and for all age groups, are nonetheless quite consistent with the post mortem findings and converge to support several conclusions.

l. Among manuscripts in the refereed literature, which by now has reached a considerable number, one can identify seven main groups that pursued issues related to neurodevelopment: 1. The Harvard group under the leadership of Kennedy and Cavines; 2. The NIH group under the leadership of Rapoport and Giedd; 3 The Stanford group under the leadership of Pfefferbaum; 4 The Hopkins group led by Denckla; 5. The UCSD group led by Jernigan; 6. The University of Utah group led by Bigler; 7. The Penn group led by Raquel E Gur and myself. Contributions from other centers such as Duke, McGill, NYU, UCLA and Toyama University in Japan have also been instrumental.

m. In one of the first studies examining segmented MRI in children and adults, Jernigan and Tallal (1990) have documented the "pruning" process proposed by Huttenlocher's work. They found that children had higher gray matter volumes than adults, indicating loss of GM during adolescence. This group has more recently replicated these results using advanced methods for image analysis (Sowell et al., 1999). Their new study also demonstrated that the pruning is most "aggressive" in prefrontal and temporo-parietal cortical brain regions.

n. The NIH group published a landmark paper in 1996, where they have reported results of a brain volumetric MRI study on 104 healthy children ranging in age from 4-18. While they did not segment the MRI data into compartments, they observed developmental changes that clearly indicated prolonged maturation beyond age 17 In a later report on this sample, where segmentation algorithms have been applied, they were able to pinpoint the greatest delay in myelination, defined as WM volume, for fronto-temporal pathways (Paus et al., 1999). Note that this finding is very

consistent with Yakovlev's projections. The NIH group went on to exploit the ability of MRI to obtain repeated measures on the same individuals. Using such longitudinal data they were able to better pinpoint the timing of pre-adolescent increase in GM that precipitated the pruning process of adolescence. Of importance to the question of maturation as defined by myelogenesis, the results indicated that the volume of WM continued to show increase up to age 22 years (Giedd et al., 1999).

o. The Harvard group developed a sophisticated procedure for MRI analysis (Filipek et al., 1994), which they applied to a sample of children with the age range of 7-11 years and compared to adults (Cavines et al., 1996). They found sex differences suggesting earlier maturation of females, and generally supported the role of WM as an index of maturation. Their results also indicated that WM shows delay in reaching its peak volume until early adulthood.

p. Another landmark study was published by the Stanford group, which examined segmented MRI on a "retrospective" sample of 88 participants ranging in age from 3 months to 30 years and a "prospective" sample of 73 healthy men aged 21 to 70 years (Pfefferbaum et al., 1994). The retrospective sample used scans available from the clinical caseload, although images were carefully selected to include only those with a negative clinical reading, while the prospective sample was recruited specifically for research and medically screened to be healthy. The results demonstrated a clear neurodevelopmental course for GM and WM, the former showing a steady decline during adolescence while the latter shows increased volume until about age 20-22 years (see Figure 6).

q. The Hopkins group used a similar approach in a sample of 85 healthy children and adolescents ranging in age from 5 to 17 years (Reiss et al., 1996). Consistent with the post mortem and the other volumetric MRI studies, they reported steady increase in WM volume with age that did not seem to peak by age 17. Unfortunately, they did not have data on older individuals (Figure 7). Their results are consistent with those of Blatter et al. (1995) from Utah, although the extensive Utah database combines ages 16-25 and therefore does not permit evaluation of changes during late adolescence and early adulthood.

r. In the only study to date that has examined segmented MRI volumes from a prospective sample of 28 healthy children aged 1 month to 10 years, as well as a small adult sample, Matsuzawa et al (2001) have applied the segmentation procedures developed by the Penn group. They have demonstrated increased volume of both GM and WM in the first postnatal months, but whereas GM volume peaked at about two years of age, the volume of WM, which indicates brain maturation, continued to increase into adulthood (Figure 8) Furthermore, consistent with the post mortem and other MRI studies that have examined this issue, the frontal lobe showed the greatest maturational lag and its myelination is unlikely completed before young adulthood.

s. While not directly examining adolescence, several studies of aging may also help shed light on development The reason is a rather ubiquitous neurodevelopmental principle: whatever "comes on board" last is also first to deteriorate with older age. In this regard, several studies have suggested that frontal and temporal cortex shows the most pronounced age-associated decline, and that this happens earlier for men

than for women (e.g., Coffee et al., 1998; Cowell et al., 1994; Gur et al., 1991, 2002; Raz et al., 1997). The possibility of further maturation occurring beyond age 17 is supported in a recent study examining age effects for a prospective sample of 116 healthy adults (57 men and 59 women, age range 18-49). As can be seen in Figure 8, volume of WM showed a positive slope for that age range (Gur et al., 2002). To examine in more detail any effects in young adulthood, defined as between the ages of 18 to 25 (and on which there is probably the least amount of published data), we have selected all individuals in this age range from that study. As can be seen in Figure 9, there is clear evidence that the maturation process, reflected in WM volume, continues into the early 20s, especially for men.

t. Physiologic studies: Functional imaging. Information on the maturational process can come not only from anatomic studies of brain structure, the focus of this review, but also from studies of brain activity or "function". Few studies have been done to examine brain maturation. Probably the main reason for the paucity of studies is that many of these methods necessitate exposure to ionizing radiation, and therefore are forbidden in healthy children. Another reason is that these studies are expensive and are usually done in very small samples. Nonetheless, several investigators have examined indices of brain maturation using functional imaging (e.g., Chugani et al., 1987; Chiron et al., 1992). These studies concur with the anatomic data. Thus, Chugani et al show that adult values are not reached by age 15 and are delayed in association cortex, while Chiron et al suggest that adult values are reached by about age 20.

u Summary and conclusions. The review of neuroanatomic studies across methods and approaches, and the few neurophysiologic studies in humans, indicates considerable convergence of findings with respect to brain maturation during childhood, adolescence and early adulthood. The overwhelming weight of the evidence supports the early post mortem studies indicating that the main index of maturation, which is the process called "myelination," is not complete until some time in the beginning of the third decade of life (probably at around age 20-22). Other maturational processes, such as the increase and subsequent elimination ("pruning") in cell number and connectivity, may be completed by late adolescence, perhaps by age 15-17. More data are needed to pinpoint the age at which these latter maturational processes are complete.

v. These results have rather profound implications for understanding behavioral development. The cortical regions that are last to mature, particularly those in prefrontal areas, are involved in behavioral facets germane to many aspect of criminal culpability. Perhaps most relevant is the involvement of these brain regions in the control of aggression and other impulses, the process of planning for long-range goals, organization of sequential behavior, consideration of alternatives and consequences, the process of abstraction and mental flexibility, and aspects of memory including "working memory." More recent evidence implicates the frontal lobes in processing aspects of morality and moral judgment. If the neural substrates of these behaviors have not reached maturity before adulthood, it is unreasonable to expect the behaviors themselves to reflect mature thought processes.

w. The brain scan techniques have demonstrated conclusively that he phenomena observed by mental health professionals in persons under 18 that would render them less morally blameworthy for offenses have a scientific grounding in neural substrates. The evidence now is strong that the brain does not cease to mature until the early 20s in those relevant parts that govern impulsivity, judgment, planning for the future, foresight of consequences, and other characteristics that make people morally culpable. Therefore, a presumption arises that someone under 20 should be considered to have an underdeveloped brain. Additionally, since brain development in the relevant areas goes in phases that vary in rate and is usually not complete before the early to mid-20s, there is no way to state with any scientific reliability that an individual 17-year-old has a fully matured brain (and should be eligible for the most severe punishment), no matter how many otherwise accurate tests and measures might be applied to him at the time of his trial for capital murder. This is similar to other physical characteristics such as height. While we know in detail the age at which the average adults reach their maximal height, predictions for individuals are not easy to make. Thus, although 18 is an arbitrary cutoff, given the ongoing development of the brain in most individuals, it must be preferred over 17 as assuring that only the most culpable are punished for capital crimes. Indeed, age 21 or 22 would be closer to the "biological" age of maturity

x. Having read portions of the Atkins v. Virginia decision, I was impressed that the very same reasons applied to mental retardation, with respect to both retribution and deterrence, apply fully to juveniles. This is not a coincidence. Most mentally retarded people have normal physical appearance and fully developed bodies. Their motor

skills are intact and they can perform most actions necessary for survival. However, for a variety of reasons their intellectual capacities, mostly those related to "executive" functions and learning, are not fully developed. These abilities are measurable by standardized tests (IQ tests) and are used to define retardation from the perspective of mental capacity. Indeed, there is a generally acceptable formula for translating IQ scores to "mental age" because the performance of mentally retarded people resembles that of average individuals at that age Conceptually mental retardation is defined developmentally - as reflected in the term "retarded"- and from a psychometric perspective the statement that individuals are "mentally retarded" is equivalent to the statement that their mental capacity is that of average juveniles. Thus, literally, it can be stated that any juvenile is retarded relative to that juvenile as an adult To illustrate, if we could build a time machine and take average 17 year old persons 4 years forward, retaining their current mental abilities, and test them, they will score retarded (of course assuming infallibility of psychological testing) While in the case of mental retardation questions regarding fallibility of psychological testing appropriately prompted the Supreme Court to require additional objective criteria for verifying retardation through developmental history, in the case of juveniles all we need is a birth certificate to determine age Behavioral scientists have long suspected that a major factor contributing to maturation of mental capacity is the development of the brain, which is the organ of mind Now neuroscientists have been able to demonstrate conclusively that mental maturation follows closely the time course of brain maturation. Thus, juveniles have to rely on the abilities of their still immature brains, and no amount of social intervention or

self-motivation can appreciably influence the biological processes involved in brain maturation.

Respectfully submitted,

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RUBEN C. GUR, PH.D. Date

Figure captions

Figure 1. Examples of the myelination process as they appear on Yakovlev's stained brain tissue for the spinal cord at lumbar level (left vertical plates) and the corpus callosum (upper horizontal plates). In the spinal cord, note the extensive darkening at dorsal compared to ventral root for a fetus at 25 weeks of gestation (top) and at term (bottom). The corpus callosum is a large body of nerve fibers connecting the two cerebral hemispheres. The leftmost section is from the brain of a baby at 6 postnatal weeks, the center shows a comparable section at one year, and the rightmost picture shows the region at 28 years. Note the increased darkness of the banana-shaped corpus callosum, indicating increased myelination (from Yakovlev and Lecours 1967, Figure 2 and 19, respectively).

Figure 2. Maturational charts for different brain regions based on post mortem tissue (from Yakovlev and Lecours 1967, Figure 1).

Figure 3. The "zones" principle of maturation, showing the late maturation of the cortical "supralimbic" region (from Yakovlev and Lecours 1967, Figure 18).

Figure 4. Brain weight (in kilograms) in relation to age based on about 10000 autopsy reports (from Dekaban and Sadowsky, 1978, Figure 1; the vertical line indicating age 21 added by the author of this review).

Figure 5. Association of age with the relative volume of gray matter (left panel) and white matter (right panel), showing decline for the former and increase for the latter (from Reiss et al., 1996, Figure 3).

Figure 6. Association of age with the cortical white matter volume (top panel) and with relative gray to white matter volume (bottom panel), showing that myelination is incomplete before the age of about 21 (from Pfefferbaum et al., 1994, Figure 3; the vertical line indicating age 21 added by the author of this review).

Figure 7. Illustration of the MRI segmentation process showing an acquired T2 weighted image (left), a proton density image (middle), and the segmented image (right) where GM is depicted in white, WM in light gray and CSF in black (from Gur et al., 1999, Figure 1).

Figure 8. Scatterplots showing the relation between age and compartmental volume (in milliliters) for healthy individuals ranging in age from 18-50 (from Gur et al., 2002)

Figure 9. A scatterplot showing the WM data (relevant to the myelogenesis index of brain maturation) in the age range of 18-16 from Figure 8 above.